

REMARKS/ARGUMENTS

Claim Amendments

By the present amendment, claim 1 has been amended to clarify that the organic polyol silane is prepared under conditions to avoid hydrolysis and polycondensation of the precursor. Support for this amendment is found, for example, on page 21, lines 28-30 and on page 22, lines 4-22. In these passages it is clear that, since the preparation of the sol gel requires "adjusting the pH of the aqueous solution of precursor so that formation of a gel occurs" and "[b]y "gel" it is meant a solution or "sol" that has lost flow" and "[t]he sols lose flow due to the hydrolysis and polycondensation of the precursor", the precursor is not hydrolysed or polycondensed prior to the sol gel formation reaction. Further in PCT patent application S.N. PCT/CA03/00790 (publication no. WO 03/2001), which teaches the preparation of organic polyol silanes, the contents of which are incorporated into the present application by reference (see page 14, lines 1-5), it is taught on page 11, lines 4-11, and in the examples, that if "exceptional care was taken to dry the solvents and precursors, it was possible to elicit transesterification to give essentially only Q^0 species – Q refers to various $Si(O_{4/2})$ species. Otherwise transesterification was accompanied by condensation.

Claim 13 has been amended to correct a typographical error by removing the second "%" in the term "50%". This amendment in no way alters the scope of this claim.

The claim amendments have been made without prejudice and without acquiescing to any of the Examiner's objections. The Applicants submit that no new matter has been entered by the present amendment and entry of the amendments is respectfully requested.

The Official Action dated September 14, 2006 has been carefully considered. It is believed that the claims and figures submitted herewith and the following comments represent a complete response to the Examiner's comments and place the present application in condition for allowance. Reconsideration is respectfully requested.

Information Disclosure Statement

The Examiner has requested a legible copy of Besanger et al. (cite number 14) that was submitted in the information disclosure statement filed on February 6, 2006. The Applicants have submitted, concurrently herewith, a supplemental information disclosure statement that includes a clearer copy of the requested publication.

Claim Rejections Withdrawn

The Applicants acknowledge and appreciate the Examiner's withdrawal of all previous claim rejections as outlined on pages 2-5 of the Office Action.

Recordation of Substance of Telephone Interview with Examiner Jung

In accordance with 37 CFR §1.113(b), the Applicants submit the following recordation of the substance of a telephone interview with the Examiner that occurred on December 13, 2006.

Present at the interview were Examiner Jung, Patricia Folkins (agent for the Applicants) and the Examiner's supervisor Long Le. There were no exhibits shown or demonstrations conducted during the interview. The merits of all of the currently rejected claims were discussed. Specific prior art that was discussed included Gill (J. Am. Chem. Soc., (1998), 120, 8587-8598) and Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421.

The Examiner's principal argument was that Gill and Gill et al. teach the use of organic polyol silanes to prepare sol gels to entrap biomolecules since Gill describes alkoxysilanes mixed with an organic polyol such as glycerol and Gill et al. teaches that poly(glyceryl) silicate (PGS, organic polyol silane) is a protein and membrane-compatible sol gel precursor that efficiently confines proteins and cells. The Examiner, in the present Office Action, admits that Gill and Gill et al. do not teach the entrapment of a liposome assembly comprising a membrane-associated molecule in sol gels prepared from PGS, however, the Examiner has rejected claims 1-9, 11 and 14-19

under 35 U.S.C. § 103(a) because the entrapment of such molecules in silica matrixes is taught by Stowell et al (U.S. Patent No. 6,284,163), therefore it would have been obvious to a person skilled in the art at the time of the present invention, to employ a liposome assembly of Stowell et al. in the method of Gill. The Examiner alleges that the motivation to combine the teachings of Gill and Stowell et al. is the advantage of using thermally and mechanically stable liposome assemblies of Stowell et al. for application in ion specific filtration and desalination, and as detectors, biosensors, biocatalysts, high performance materials and optical and diagnostic devices with a reasonable expectation of success, as Gill et al. teaches that PGS is compatible with protein and membranes in an encapsulation process.

The Applicants principal argument was that at every location in Gill and Gill et al. where the preparation of PGS is described, it is clear that this precursor molecule is already partially hydrolysed and condensed prior to contact with a biological material for entrapment. The Applicants argue that, in the preparation of their polyol modified silane precursors, care is take to avoid conditions that would lead to the hydrolysis and condensation of their material, accordingly, their precursor molecules are chemically and structurally very different from Gill and Gill et al.'s PGS. The Applicants informed the Examiner that they have performed side-by-side sol gel forming reactions under identical conditions with PGS and diglyceryl silane (DGS, an organic polyol silane within the scope of the present invention) and have found these materials produce vastly different products. This information was provided in declaration form in the examination of a related, co-pending patent application (U.S. Patent Application S.N. 10/814,123) and can also be provided in the present application if the Examiner deems it would be helpful.

The Examiner suggested that if the claims are amended so that it is clarified that the organic polyol silane is prepared using a method that avoids hydrolysis and polycondensation of the precursor then this should distinguish the method of the present invention from that of Gill and Gill et al. The Examiner further suggested that it would be helpful for the above-mentioned declaration be submitted.

New Claim Rejections

35 U.S.C. §103(a)

The Examiner has rejected claims 1-9, 11 and 14-19 under 35 U.S.C. §103(a) as being unpatentable over by Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Gill et al. (J. Am. Chem. Soc. 1998, Vol. 120, pp.8587-8598) and Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001). The Applicants respectively traverse this rejection for the reasons that follow.

The Examiner's objection is based on the contention that Gill teaches a method of immobilizing membrane associated molecules in silica matrixes by combining these molecules with a protein- and membrane-compatible sol-gel precursor and, further that Gill teaches that the protein- and membrane-compatible sol-gel precursor may be an organic polyol silane. The latter conclusion is based on the indication in Gill that alkoxy silanes can be mixed with an organic polyol such as glycerol (pp.3406-9 and Figure 1 on p. 3407). The Applicants strongly disagree with the Examiner's allegation that Gill (or Gill et al.) teaches an organic polyol silane as a precursor to protein- and membrane-compatible sol-gels for the reasons that follow.

On page 3406 of Gill, it is taught that the procedure for bioencapsulation involves (1) preparing an aqueous sol composed of a partially or fully hydrolyzed alkoxyasilane and (2) mixing the precursor sol with the biological. In one aspect Gill teaches that the precursor sol may be prepared as follows:

Alkoxysilanes are 50-75% hydroly[zed] and transesterified with glycerol under acidic, basic, or alkoxide catalysts in alcohol solvent, to form water-soluble isolable poly(glyceryl silicates) and poly (glyceroxysiloxanes) which are dissolved in water.

Further, in Figure 1 it is taught, again, that simple alkoxysilanes are partially or fully hydrolyzed to form poly(glyceryl silicates), poly(glyceryl metallosilicates),

poly(alkylglyceroxysilanes) or poly(oxometalloalkylglyceroxysilanes) which are dissolved in water to provide a "precursor gel solution" to which a biomolecule is added for entrapment.

Further in Gill et al. it is taught on page 8595-8596, that the preparation of methyl/ethyl ester and polyol ester precursors is performed as follows:

Poly(methyl silicate) (PMS) and poly(glyceryl silicate) (PGS): TEOS (0.48 mol) was mixed with ethanol (50 mL), and hydrochloric acid (10.4 mL of 0.25 M) was added over 30 min with vigorous stirring; then the mixture was heated to 70 °C for 15 h. Rotary evaporation at 35 °C provided PMS of composition $\text{SiO}_{1.1-1.2}(\text{OMe})_{1.6-1.8}$ as a clear, viscous liquid. PGS was obtained by adding glycerol (0.38 mol) to the reaction mixture over 1 h, heating to 50 °C, and stirring for a further 40 h. [...] FAB-MS indicated that the product consisted mostly of glyceryl-bridged linear oligomeric polysilicates of DP 5-9. Various glyceryl silicates ("SiGlc₂₋₄") and poly(glyceryl silicates) (" $\text{SiO}_{0.5-1.5}\text{-Glc}_{0.5-2}$ ") were prepared by this method.

Therefore, at every point in Gill and Gill et al. where it is taught that glycerol may be combined with an alkoxysilane, this combination is only done with an alkoxy silane that is partially or fully hydrolysed into polymeric species. Accordingly, to more completely define the present invention, and to highlight the differences between the present invention and the teachings of Gill and Gill et al., the Applicants have amended claim 1, and accordingly all of the claims dependent thereon, including claim 2-9, 11 and 14-19, to specify that the organic polyol silane is prepared under conditions to avoid hydrolysis and polycondensation the precursor.

Still further, the Applicants submit that it is well known in the art that the partially or fully hydrolysed species described in Gill and Gill et al. are structurally fundamentally different from, and would therefore have different reactivities than, the non-oligomeric polyol silanes of the present invention. The Applicants have confirmed this fact with experimental evidence. This evidence has been provided in the attached declaration of Michael A. Brook under 37 CFR §1.132, submitted in co-pending patent application S.N.

10/814,123, where the non-equivalence of polyglyceryl silicate and polyol silanes (specifically diglycerylsilane or DGS), as well as alkoxysilanes, has been proven by performing sol gel reactions under identical conditions and showing that these three classes of precursor compounds do not produce the same reaction product.

As noted in the declaration, the Applicants performed sol gel reactions under equivalent conditions with diglycerylsilane (a precursor within the scope of the present invention), polyglyceryl silicate (the precursor used in Gill) and tetraethoxysilane (a precursor otherwise known in the art). These reactions were performed near the extreme range of pH that is taught in the present application (i.e at pH 5.5 and 11) under conditions otherwise commensurate in scope Gill and Gill et al. The data clearly shows the significant difference between the reactivity and resulting products produced by these three precursors. The material of the present invention was the only one that produced macroporous siliceous materials under these conditions.

The Applicants submit that the evidence presented in the attached declaration clearly shows that the non-hydrolysed and non-condensed polyol silane precursors utilized in the method of the present invention are not only novel over the teachings in the cited art, but that they are also non-obvious as a person skilled in the art would not have been motivated to replace the precursor compounds utilized in Stowell et al. with the polyol silane precursors utilized in the present application, in light of the teachings of Gill and Gill et al. This is because Gill teaches the use of already partially hydrolyzed and condensed precursor materials which (as proven by the Applicants' experiments) are not equivalent to the non-polymerized species used by the Applicants.

While the motivation to combine references to arrive at a claimed invention need not be the same one that was relied on by the inventors, the courts held *In re Dillon* that

[t]he art provided the motivation to make the claimed compositions *in the expectation that they would have similar properties*. (Emphasis added)
919 F.2d at 693, 16 USPQ2d at 1901

Therefore, for there to be motivation to combine the teachings of Stowell with that of Gill and Gill et al., there would have to be some evidence in the art that there is a reasonable expectation that the material used by Gill and Gill et al and that used by the Applicants would have similar properties. Accordingly, there may some merit to the Examiner's argument if Gill and Gill et al. taught the use of the same class of precursor as that used by the present Applicants. However, as noted above, Gill does not teach exchanging alkoxy groups with glyceryloxy groups on a non-hydrolysed and non-condensed polyol silane. Gill teaches the use of a partially hydrolyzed and condensed material (polyglyceryl silicate or PGS) as a precursor in the preparation of sol gels. This material is not equivalent to the monomeric alkoxysilanes utilized by the Applicants.

Since all of claims 1-9, 11 and 14-19 require the use of a non-hydrolysed and non-condensed polyol silane precursor in the method of immobilizing membrane-associated molecules, and since none of the prior art teaches or suggests the existence, let alone the use of such materials, the Applicant submit that claims 1-9, 11 and 14-19 are in compliance with 35 U.S.C. §103(a).

In light of the above, the Applicants request that the Examiner's rejection of claims 1-9, 11 and 14-19 under 35 U.S.C. §103(a) be withdrawn.

The Examiner has rejected claim 10 under 35 U.S.C. §103(a) as being unpatentable over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Gill et al. (J. Am. Chem. Soc. 1998, Vol. 120, pp.8587-8598) and Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001) as applied to claim 9 above, and further in view of Madden (U.S. Patent No. 4,963,287).

Claim 10 depends indirectly on claim 1 and further specifies that the liposome comprises the phospholipid 1,2-dioleoyl-*sn*-glycero-3-phosphocholine (DOPC). The Examiner contends that this feature is taught by Madden, therefore it would have been obvious to a person of ordinary skill in the art at the time of the present invention, to include in the method of Gill, in view of Gill et al. and Stowell et al., a method of forming

a liposome assembly using DOPC as taught by Madden in order to form a liposome assembly without harsh treatments and to enhance insertion of membrane proteins and peptides with a reasonable expectation of success.

The Applicants have amended claim 1, and accordingly claim 10 dependent thereon to clarify that the organic polyol silane is prepared under conditions to avoid hydrolysis and polycondensation of the precursor. As argued above, this amendment serves to further distinguish the present invention from Gill and Gill et al. so that the claims submitted herewith are not obvious over Gill in view of Gill et al. and Stowell. Madden does not teach or suggest to use as a precursor, an organic polyol silane prepared under conditions to avoid hydrolysis and polycondensation of the precursor, accordingly this reference does not fill the gaps left in the art by the teachings of Gill in view of Gill et al. and Stowell et al. Claim 10 is therefore not obvious over Gill in view of Gill et al. and Stowell et al. further in view of Madden.

In light of the above, the Applicants request that the Examiner's rejection of claim 10 under 35 U.S.C. §103(a) be withdrawn.

The Examiner has rejected claims 12 and 13 under 35 U.S.C. §103(a) as being unpatentable over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Gill et al. (J. Am. Chem. Soc. 1998, Vol. 120, pp.8587-8598) and Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001) as applied to claims 1 and 11 above, and further in view of Lapidot et al. (U.S. PG Pub. No. US 2002/0064541) and Smith et al. (J. Am. Chem. Soc. 2002, 124:4247-4252).

Claims 12 and 13 depend indirectly on claim 1 and further specify that the gel is dried in an aqueous buffer, optionally comprising a humectant (claim 12) or comprising about 5% to about 50 % (v/v) of glycerol (claim 13). The Examiner contends that these features are taught by Lapidot et al. and Smith et al., therefore it would have been obvious to a person of ordinary skill in the art at the time of the present invention, to include in the method of Gill, in view of Gill et al. and Stowell et al., a use of humectant

such as glycerol in a buffer solution as taught by Smith et al. to use during the drying process as taught by Lapidot et al. in order to control the surface nature of the sol gel matrix and remove ethanol produced during the gelation reaction and during the aging and drying steps with a reasonable expectation of success.

The Applicants have amended claim 1, and accordingly claims 12 and 13 dependent thereon to clarify that the organic polyol silane is prepared under conditions to avoid hydrolysis and polycondensation of the precursor. As argued above, this amendment serves to further distinguish the present invention from Gill and Gill et al. so that the claims submitted herewith are not obvious over Gill in view of Gill et al. and Stowell. Lapidot et al. and Smith et al. do not teach or suggest to use as a precursor, an organic polyol silane prepared under conditions to avoid hydrolysis and polycondensation of the precursor, accordingly these references do not fill the gaps left in the art by the teachings of Gill in view of Gill et al. and Stowell et al. Claims 12 and 13 are therefore not obvious over Gill in view of Gill et al. and Stowell et al. further in view of Lapidot et al. and Smith et al.

The Applicants further note that in the method of the present invention, there is no ethanol produced as a side product, accordingly a person skilled in the art would not have been motivated by the teachings in Smith et al. to utilize glycerol during the washing step.

In light of the above, the Applicants request that the Examiner's rejection of claims 12 and 13 under 35 U.S.C. §103(a) be withdrawn.

The Examiner has rejected claims 20 and 21 under 35 U.S.C. §103(a) as being unpatentable over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Gill et al. (J. Am. Chem. Soc. 1998, Vol. 120, pp.8587-8598) and Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001) as applied to claims 1 and 15-19 above, and further in view of Keeling-Tucker et al. (Chem. Mater. 2001, 13:3331-3350).

Claims 20 and 21 depend indirectly on claim 1 and further specify that the water soluble polymer is PEO, PEO-NH₂ and polyNIPAM (claim 20) and PEO (claim 21). The Examiner contends that the use of PEO as an additive is taught by Keeling-Tucker, therefore it would have been obvious to a person of ordinary skill in the art at the time of the present invention, to include in the method of Gill, in view of Gill et al. and Stowell et al., the use of the additive PEO as taught by Keeling-Tucker in order to provide segregation into independent phases prior to gelation with a reasonable expectation of success.

The Applicants have amended claim 1, and accordingly claims 20 and 21 dependent thereon to clarify that the organic polyol silane is prepared under conditions to avoid hydrolysis and polycondensation of the precursor. As argued above, this amendment serves to further distinguish the present invention from Gill and Gill et al. so that the claims submitted herewith are not obvious over Gill in view of Gill et al. and Stowell. Keeling-Tucker does not teach or suggest to use as a precursor, an organic polyol silane prepared under conditions to avoid hydrolysis and polycondensation of the precursor, accordingly this reference does not fill the gaps left in the art by the teachings of Gill in view of Gill et al. and Stowell et al. Claims 20 and 21 are therefore not obvious over Gill in view of Gill et al. and Stowell et al. further in view of Keeling-Tucker.

In light of the above, the Applicants request that the Examiner's rejection of claims 20 and 21 under 35 U.S.C. §103(a) be withdrawn.

The Examiner has rejected claims 20-23 under 35 U.S.C. §103(a) as being unpatentable over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Gill et al. (J. Am. Chem. Soc. 1998, Vol. 120, pp.8587-8598) and Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001) as applied to claims 1 and 115-19 above, and further in view of Leung et al. (U.S. Patent No. 6,204,202).

Claims 20-23 depend indirectly on claim 1 and further specify that the water soluble polymer is PEO, PEO-NH₂ and polyNIPAM (claim 20), PEO (claim 21), PEO with a molecular of between about 2000-100,000 Da and PEO with a molecular weight of about 10000Da. The Examiner contends that the use of PEO having a molecular weight in the range of about 200 to 2,000,000) Da as an additive is taught by Leung et al., therefore it would have been obvious to a person of ordinary skill in the art at the time of the present invention, to include in the method of Gill, in view of Gill et al. and Stowell et al., the use of the additive PEO, in particular with a molecular weight in the range of 2000-100,000 as taught by Leung et al. in order to make silica nanoporous films (such as sol gels) with sufficient mechanical strength that are also optimized to have a desirably low and stable dielectric constant, without the need for further processing to make the film hydrophobic, with a reasonable expectation of success.

The Applicants have amended claim 1, and accordingly claims 20-23 dependent thereon to clarify that the organic polyol silane is prepared under conditions to avoid hydrolysis and polycondensation of the precursor. As argued above, this amendment serves to further distinguish the present invention from Gill and Gill et al. so that the claims submitted herewith are not obvious over Gill in view of Gill et al. and Stowell. Leung et al. does not teach or suggest to use as a precursor, an organic polyol silane prepared under conditions to avoid hydrolysis and polycondensation of the precursor, accordingly this reference does not fill the gaps left in the art by the teachings of Gill in view of Gill et al. and Stowell et al. Claims 20-23 are therefore not obvious over Gill in view of Gill et al. and Stowell et al. further in view of Leung et al.

In light of the above, the Applicants request that the Examiner's rejection of claims 20-23 under 35 U.S.C. §103(a) be withdrawn.

The Examiner has rejected claims 24 and 25 under 35 U.S.C. §103(a) as being unpatentable over Gill (Chem. Mater. Web Release Date of July 4, 2001, Vol. 13, pp. 3404-3421) in view of Gill et al. (J. Am. Chem. Soc. 1998, Vol. 120, pp.8587-8598) and

Stowell et al. (U.S. Patent No. 6,284,163, Sept. 4, 2001) as applied to claims 1, 15 and 16 above, and further in view of Delamarche et al. (Langmuir, 2003, 19:8749-8758).

Claims 24 and 25 depend indirectly on claim 1 and further specify that the additive is a compound of Formula I (claim 24) and a compound of Formula 5 (claim 25). The Examiner contends that the use of PEO-silane in a sol gel polymer ink is taught by Delamarche et al., therefore it would have been obvious to a person of ordinary skill in the art at the time of the present invention, to include in the method of Gill, in view of Gill et al. and Stowell et al., the use of PEO-silane as taught by Delamarche et al. in order to construct a stable hydrophilic structure with a reasonable expectation of success.

The Applicants have amended claim 1, and accordingly claims 24 and 25 dependent thereon to clarify that the organic polyol silane is prepared under conditions to avoid hydrolysis and polycondensation of the precursor. As argued above, this amendment serves to further distinguish the present invention from Gill and Gill et al. so that the claims submitted herewith are not obvious over Gill in view of Gill et al. and Stowell. Delamarche et al. does not teach or suggest to use as a precursor, an organic polyol silane prepared under conditions to avoid hydrolysis and polycondensation of the precursor, accordingly this reference does not fill the gaps left in the art by the teachings of Gill in view of Gill et al. and Stowell et al. Claims 24 and 25 are therefore not obvious over Gill in view of Gill et al. and Stowell et al. further in view of Delamarche et al.

In light of the above, the Applicants request that the Examiner's rejection of claims 24 and 25 under 35 U.S.C. §103(a) be withdrawn.

Claims 1 and 3-25 have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9, 16, 37, 38, 39, 41, 47, 49, and 51 of co-pending application no. 10/814,123 in view of Stowell et al. (U.S. Patent No. 6,284,163).

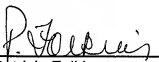
The Applicants have submitted herewith a terminal disclaimer which renders the Examiner's rejection of claims 1 and 3-25 moot.

In light of the above, the Applicants request that the Examiner's rejection of claims 1 and 3-25 under the judicially created doctrine of obviousness-type double patenting be withdrawn.

Early and favorable action on the merits is awaited. Should the Examiner deem it beneficial to discuss the application in greater detail, the Examiner is invited to contact the undersigned by telephone at (416) 957-1683 at the Examiner's convenience.

Respectfully submitted,

BERESKIN & PARR

By 

Patricia Folkins
Reg. No. 51,933

Bereskin & Parr
Box 401, 40 King Street West
Toronto, Ontario
Canada M5H 3Y2
Tel: 416-957-1682
Fax: 416-361-1398